GCCTGCCGCTCCCGGGGACCCGATCCTACCCTGGGTGCGGGGCAGAGCGGGCATGGCCCGTCTGGGGACCGCCTGCC CTTCTCGCCTTCAATGCATGAAGACCTTAGGGTGGAGGAGCAGGAACAGCAGGAGCCGCACCAGGAGCCACAGAA AATAGCAACAGAAAAGGCAGAAGAAGCAAGAATCTTGAGAAAGCTGCCAGTGATGACCATGGTGTCCCTGTGGCTCA TGAGGATGTCAGAGAGAGTTGCCCACCTCTTGGTCTGGAAACATTAAAAATCACAGACTTCCAGCTGCATGCCTCCA GATGGGGCTTGGTGTGCTGGTAGGAACGACTTGCATCAGTGGATCGAAGTGGATGCCCGGCGCCTGACCAAGTTCAC AGGGGTCATTACCCAAGGAAGGAACTCTCTCTGGCTGAGTGACTGGGTGACATCCTATAAAGTCATGGTGAGCAATG ACAGCCACACATGGGTTACTGTGAAGAATGGATCTGGCGACATGATATTTGAAGGAAACAGTGAGAAGGAGATTCCT GTGCTCAATGAGCTGCCAGTCCCCATGGTGGCCCGCTACATTCGCATAAACCCTCAGTCCTGGTTTGATAACGGGAG CATCTGCATGAGGATGGAGATCTTGGGCTGCCCACTGCCGGATCCTAATAACTATTATCACCGACGTAATGAGATGA CCACCACGGATGACCTGGATTTTAAGCACCACAACTATAAGGAAATGCGCCAGTTGATGAAGGTTGTCAATGAAATG TGCCCCAATATTACCAGGATTTACAACATTGGCAAAAGCCACCAGGGCCTGAAATTGTATGCGGTAGAGATCTCTGA GAGGAGACTCGAATCCACATTCTACCCTCCATCATCCTGATGGCTATGAGAAGGCCTATGAAGGAGGTTCCGAGTT TCTGGGAGGCAGAGGACCAGCAGAATGCCCCAAGGAAGGTCCCCAACCACTACATTGCCATCCCTGAGTGGTTTCTG CAACCTACAGGGGGGTGAGCTGGTCGTGGCATACCCCTATGACATGGTGCGGTCCCTGTGGAAGACCCAGGAGCACA CCCCAACACCTGATGATCATGTGTTCCGCTGGCTGGCGTATTCCTACGCCTCCACTCACCGCCTCATGACAGATGCC AGGAGGCGAGTGTGCCACACGGAAGATTTTCAGAAGGAGGAGGGCACCGTCAATGGGGCTTCCTGGCACACAGTGGC TGGAAGTCTAAACGATTTCAGCTACCTCCATACAAACTGCTTTGAGCTGTCCATCTACGTGGGCTGTGATAAATACC TGACATCCGGACAGCCAGCGATGGGGATTACTGGCGTCTACTGAACCCTGGCGAATATGTGGTCACAGCCAAGGCGG AAGGCTTTATCACTTCCACCAAGAACTGCATGGTTGGCTATGATATGGGAGCTACTCGGTGTGACTTCACCCTCACA GAAGCTGCGGGGACGGAAAAGGCCGCGCGTGGGTGACCCTGTCGGACACTTGAGACATACCCCAGACCGTGCAAAT AAAAATCCACTCCAGTAGTAAAAAAA

(SEO ID NO:1)

MARLGTACPALALALALVAVALAGVRAQGAAFEEPDYYSQELWRRGRYYGHPEPEPELFSPSMHEDLR VEEQEQQEPHQQGHRTPKKAIKPKKAPKREKLVAETPPPGKNSNRKGRRSKNLEKAASDDHGVPVAHEDV RESCPPLGLETLKITDFQLHASTSKRYGLGAHRGRLNIQAGINENDFYDGAWCAGRNDLHQWIEVDARRL TKFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIFEGNSEKEIPVLNELPVPMVARYIR INPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTTTDDLDFKHHNYKEMRQLMKVVNEMCPNITRIY NIGKSHQGLKLYAVEISDHPGEHEVGEPEFHYIAGAHGNEVLGRELLLLLLHFLCQEYSAQNARIVRLVE ETRIHILPSLNPDGYEKAYEGGSELGGWSLGRWTHDGIDINNNFPDLNSLLWEAEDQQNAPRKVPNHYIA IPEWFLSENATVATETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDMVRSLWKTQEHTPTPDDHVFRWLA YSYASTHRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHESEL PEEWENNRESLIVFMEQVHRGIKGIVRDLQGKGISNAVISVEGVNHDIRTASDGDYWRLLNPGEYVVTAK AEGFITSTKNCMVGYDMGATRCDFTLTKTNLARIREIMETFGKQPVSLPSRRLKLRGRKRRQRG (SEQ ID NO:2)

Figure 1

## <u>underlined</u> = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[AGGCTGTCCCACCACCATCTGCACCCGCTGCAGCGCCCGCGCCCCTGTCCCGCGCCGT AGTCGTCATTTGTAGCCCGCCTGCCGCTCCCGGGGACCCGATCCTACCCTGGGTGCGGG CAGAGCGGCATGGCCCGTCTGGGGACCGCCTGCCCTGCGCTGGCGCTGGCCCTGGCACT TGTGGCGGTGGCCTGGCTGGAGTCAGAGCCCAGGGCGCAGCCTTCGAGGAGCCTGACTA TTACAGCCAGGAGCTCTGGCGGCGCGCGCTATTATGGGCATCCGGAGCCTGAGCCGGA GCCGGAGCTCTTCTCGCCTTCAATGCA] TGAAGACCTTAGGGTGGAGGAGCAGGAACAGC <u>AGGAGCCGCACCAGGAGGCCACAGAACTCCCAAGAAGGCCATCAAGCCCAAGAAGGCTC</u> CCAA [GAGGGAGAAGTTAGTTGCAGAGACGCCTCCACCAG] GTAAAAATAGCAACAGAAA AGGCAGAAGAAGCAAGAATCTTGAGAAAGCTGCCAGTGATGACCATGGTGTCCCTGTGGC TCATGAGGATGTCAGAGAGTTGCCCACCTCTTGGTCTGGAAACATTAAAAATCACAGA CTTCCAGCTGCATGCCTCCACATCGAAGCGTTATGGCCTGGGAGCCCACCGGGGGAGACT CAACATCCAGGCAGCATTAATGAAAATGACTTTTACGATGGGGCTTGGTGTGCTGGTAG GAACGACTTGCATCAGTGGATCGAAGTGGATGCCCGGCGCCTGACCAAGTTCACAGGGGT CATTACCCAAGGAAGGAACTCTCTCTGGCTGAGTGACTGGGTGACATCCTATAAAGTCAT GGTGAGCAATGACAGCCACACATGGGTTACTGTGAAGAATGGATCTGGCGACATGATATT TGAAGGAAACAGTGAGAAGGAGATTCCTGTGCTCAATGAGCTGCCAGTCCCCATGGTGGC  $\verb|CCGCTACATTCGCATAAACCCTCAGTCCTGGTTTGATAACGGGAGCATCTGCATGAGGAT|\\$ GGAGATCTTGGGCTGCCCACTGCCGGATCCTAATAACTATTATCACCGACGTAATGAGAT GACCACCACGGATGACCTGGATTTTAAGCACCACAACTATAAGGAAATGCGCCAGTTGAT GAAGGTTGTCAATGAAATGTGCCCCAATATTACCAGGATTTACAACATTGGCAAAAGCCA CCAGGGCCTGAAATTGTATGCGGTAGAGATCTCTGACCATCCTGGGGAACATGAAGTTGG  ${\tt TGAGCCCGAGTTCCACTACATCGCAGGGGCCCACGGCAATGAGGTTCTGGGACGAGAACT}$ CCGCTTGGTGGAGGACTCGAATCCACATTCTACCCTCCAATCCTGATGGCTATGA GAAGGCCTATGAAGGAGGTTCCGAGTTGGGAGGCTGGTCCCTGGGACGTTGGACCCATGA TGGCATCGATATCAACAACAACTTTCCGGATTTAAACTCGCTGCTCTGGGAGGCAGAGGA CCAGCAGAATGCCCCAAGGAAGGTCCCCAACCACTACATTGCCATCCCTGAGTGGTTTCT CCCGTTTGTGCTGGGAGGCAACCTACAGGGGGGTGAGCTGGTCGTGGCATACCCCTATGA CATGGTGCGGTCCCTGTGGAAGACCCAGGAGCACCCCAACACCTGATGATCATGTGTT CCGCTGGCTGGCGTATTCCTACGCCTCCACTCACCGCCTCATGACAGATGCCAGGAGGCG AGTGTGCCACACGGAAGATTTTCAGAAGGAGGAGGGCACCGTCAATGGGGCTTCCTGGCA CACAGTGGCTGGAAGTCTAAACGATTTCAGCTACCTCCATACAAACTGCTTTGAGCTGTC TAACCGGGAGTCTCTGATTGTGTTCATGGAGCAGGTTCATCGAGGCATCAAAGGCATAGT GAGAGATTTACAAGGGAAAGGGATTTCAAATGCTGTCATCTCTGTGGAAGGTGTTAACCA TGACATCCGGACAGCCAGCGATGGGGATTACTGGCGTCTACTGAACCCTGGCGAATATGT GGTCACAGCCAAGGCGGAAGGCTTTATCACTTCCACCAAGAACTGCATGGTTGGCTATGA TATGGGAGCTACTCGGTGTGACTTCACCCTCACAAAGACCAACCTGGCTAGGATAAGAGA AATTATGGAGACATTTGGGAAGCAGCCTGTCAGCCTACCCTCCAGGCGCCTGAAGCTGCG GGGACGGAAAAGGCGGCAGCGTGGGTGACCCTGTCGGACACTTGAGACATACCCCAGACC GTGCAAATAAAAATCCACTCCAGTAGTAAAAAAA (SEQ ID NO:1)

Figure 2A

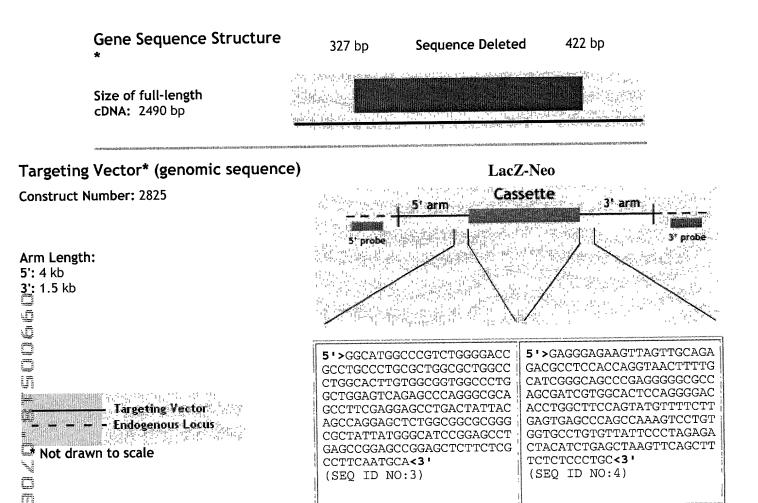


Figure 2B

A 4

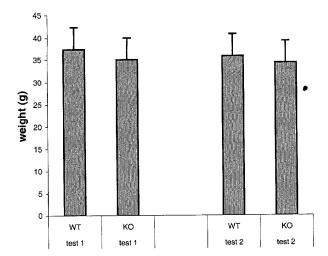


Figure 3

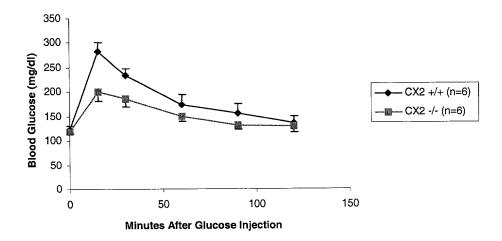


Figure 4